193

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:	)	
	)	
SKLAR *et al.*	)	**Examiner: Brannock, M.**
	)	
Serial Number: 09/370,358	)	**Art Unit: 1646**
	)	
Filed: August 9, 1999	)	
	)	
For: DISPLAY OF RECEPTORS AND ANALYSIS OF BINDING INTERACTIONS AND DRUG LIBRARIES	)	**Docket No.: UNME-0078-1**

#31 B.J. 5/27/03

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPELLANTS' BRIEF ON APPEAL

Sir:

This is further to Appellants'/Applicants' Notice of Appeal, February 19, 2003. The date for filing an Appeal Brief has been extended to May 19, 2003, by filing a petition for a one-month extension of time and paying the appropriate fee. Applicants submit herewith this brief in support of their appeal to the Board of Appeals and Patent Interferences from the Final Action dated November 18, 2002 (Final Action) that rejected claims 1-6, 8-13, 15-17, 48, 51 and 53-57, which are all of the currently pending claims. This brief is being submitted in triplicate, together with the requisite fee of $160.00.

1. REAL PARTY IN INTEREST

The above-identified application has been assigned by all inventors to The Science & Technology Corporation at the University of New Mexico, which is the real party in interest in the above-identified application.

2. Related Appeals and Interferences

There are currently no appeals or interferences known to the Applicants, the Applicants' legal representative, or the assignee that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

3. Status of Claims

Claims 1-6, 8-13, 15-17, 48, 51 and 53-57 are currently pending. (*See* Appendix A). All of the currently pending claims have been finally rejected and are the subject of this appeal.

4. Status of Amendments

Applicants filed a Request for Continued Examination and Amendment on August 21, 2002, and the August 21, 2002 Amendment has been entered as indicated on page 2 of the Final Action. The Final Action rejected all claims currently pending in the present application and is the subject of this appeal. No Amendment has been entered or filed after the Final Action.

5. Summary of the Invention

With respect to the claims on appeal, in one embodiment the present application claims a method for non-cellular analysis and display of 7-transmembrane receptors. The method comprises the steps of: incorporating an attachment tether to a receptor,

solubilizing the receptor and presenting the receptor in conjunction with a support. The support comprises at least one substrate selected from the group consisting of silica bead substrates, latex bead substrates and other bead substrates appropriate for flow cytometry. The receptor in conjunction with the support is analyzed with a flow cytometer in real-time.

In a second embodiment, the present application claims a method for non-cellular display of 7-transmembrane receptors. The method comprises the steps of: incorporating an attachment means to a receptor, solubilizing the receptor, presenting the receptor in conjunction with a support, presenting at least one ligand to bind to the receptor, combining the receptor and ligand to accomplish binding while the receptor is bound to the support; and sorting the bound receptor ligand pairs by fluorescence and using flow cytometry to analyze the fluorescence and binding interactions in real-time. The ligand is known to bind to the receptor.

6. ISSUES

(1) Whether the rejection under 35 U.S.C. § 103(a) of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower) should be withdrawn as improper and claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 allowed, because the combination of Dower with Baumbach is improper.

(2) Whether the rejection under 35 U.S.C. § 103(a) of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower) should be withdrawn as improper and claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 allowed, because the combination of Dower with Baumbach fails to teach or suggest the methods of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57.

(3) Whether the rejection under 35 U.S.C. § 103(a) of claims 2-5 and 8 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower), and further in view of Robeva should be withdrawn as improper and claims 2-5 and 8 allowed, because the combination of Robeva with Dower and Baumbach is improper.

(4) Whether the rejection under 35 U.S.C. § 103(a) of claims 2-5 and 8 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower), and further in view of Robeva should be withdrawn as improper and claims 2-5 and 8 allowed, because the combination of Robeva with Dower and Baumbach fails to teach or suggest the methods of claims 2-5 and 8.

(5) Claims 1-6, 8-13, 15-7, 48, 51, and 53-57 have been rejected upon facts within the personal knowledge of the Examiner, and Applicants hereby request under

37 C.F.R. § 1.104(d)(2) that the Examiner provide an affidavit supporting the Examiner's assertions used as a basis for the rejections of these claims.

7. GROUPING OF CLAIMS

(1) With respect to the rejection under 35 U.S.C. § 103(a) of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower), claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 do not stand or fall together for the reasons discussed below.

(2) With respect to the rejection under 35 U.S.C. § 103(a) of claims 2-5 and 8 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower), and further in view of Robeva, claims 2-5 and 8 stand or fall together.

8. ARGUMENT

(1) Whether the rejection under 35 U.S.C. § 103(a) of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower) should be withdrawn as improper and claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 allowed, because the combination of Dower with Baumbach is improper.

In discussing why a person of ordinary skill in the art would combine Dower with Baumbach, the Final Action states at pages 4-5 that:

> [I]t would have been obvious to one of ordinary skill in the art, at the time the invention was made, and with reasonable expectation of success to use beads as the solid support and to separate the receptor-ligand pairs by flow cytometry as taught by U.S. Patent No. 5639603 [Baumbach], when practicing the assay of soluble receptors attached to solid supports as taught by U.S. Patent No. 5583010 (Dower). The motivation to do so was provided by U.S. Patent No. 5639603 wherein it is taught that "by adopting cell sized solid supports or beads on can use ***flow cytometry*** for high sensitivity receptor binding analysis and facile bead manipulation" (see col 31, L47-54) (emphasis added).

The above statement in the Office Action indicates that the rejection of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 based on Baumbach ***in view*** of Dower is *prima facie* improper because the stated motivation for combining Dower with Baumbach is found in Dower not Baumbach. For a proper rejection to be based on Baumbach ***in view*** of Dower, the motivation should be found in Baumbach not Dower. However, as stated in the Office Action at page 4, Baumbach "appears to be silent with regard to flow cytometry" so Baumbach would provide not motivation to a person of ordinary skill in the art to look to Dower which relates to flow cytometry. Therefore, Dower cannot be properly combined with Baumbach.

Furthermore, the Office Action fails to provide any grounds why a person of ordinary skill in the art would be motivated to combine Baumbach with Dower. As stated in the Office Action at page 4, Dower "teaches the general applicability of ***flow cytometry*** to the sorting of isolated solubilized receptors and their bound ligands, wherein the solid supports are beads appropriate for ***flow cytometry*** and for library screening" (emphasis added). Therefore, a person of ordinary skill in the art just possessing Dower would have no motivation to look to Baumbach, which, as the

Office Action admits, is silent with respect to flow cytometry.

For the above reasons, the rejection under 35 U.S.C. § 103(a) of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower) should be withdrawn as improper and claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 allowed, because the combination of Dower with Baumbach is improper

(2) Whether the rejection under 35 U.S.C. § 103(a) of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower) should be withdrawn as improper and claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 allowed, because the combination of Dower with Baumbach fails to teach or suggest the methods of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57.

With respect to claim 1, claim 1 claims a method for non-cellular analysis and display of 7-transmembrane receptors comprising a) incorporating an attachment tether to a receptor; b) solubilizing the receptor; and c) presenting the receptor in conjunction with a support, wherein said support comprises at least one substrate selected from the group consisting of silica bead substrates, latex bead substrates and other bead substrates appropriate for flow cytometry, and wherein the receptor in conjunction with a support is analyzed with a flow cytometer in real-time. However, at a minimum, the Baumbach

and Dower fail to teach or suggest analyzing with a flow cytometer in real-time as recited in claim 1, and therefore, claim 1 is patentable over Baumbach and Dower, alone or in combination.

As admitted in the Office Action at page 4, Baumbach "appears to be silent with regard to flow cytometry." Thus, in an attempt to remedy the deficiencies of Baumbach, Dower is cited for teaching the general applicability of flow cytometry to the sorting of receptors and bound ligands. However, the general methodology and the flow cytometric analysis of Dower is very different from that recited in claim 1.

Dower provides for solubilization of a molecular or ligand library and display of the library on beads. The bead-bound library is then placed in contact with labeled receptors. A washing step is employed to remove unbound or non-specifically bound receptors. Then, a flow cytometer is used to identify and isolate individual beads showing high fluorescence. (*See* Dower, Col. 31, line 42+).

Claim 1 differs in several respects. Dower solubilizes and binds a ***ligand library*** to a bead. However, claim 1 recites the solubilization and subsequent attachment via a tether of a ***receptor*** to a bead. The solubilization and binding of the ***receptor*** allows the flow cytometric analysis to be carried out in real-time (*i.e.*, without the need for a washing step.) On the other hand, the binding of receptors in solution to an unknown ligand library discussed in Dower, requires a washing step to remove unbound or non-specifically bound receptors before analyzing with a flow cytometer. This extra step (or steps) adds time and the possibility for error in the analysis step. Through this process, Dower seeks to determine the identity of the bound ligand within the ligand library and

thus seeks the areas of high fluorescence for isolation. However, in claim 1, it is a known receptor that is bound to the bead and it is the interaction with the bound receptor that is analyzed.

At pages 5-6 of the Office Action, the Examiner states:

> The wash step contemplated by Dower at line 60 col 31 is inherent to that particular application of the general method. If one were using the method of Dower to analyze the interaction between a receptor and it's known ligand, as Applicant points out, then a wash step would obviously not be required. The purpose of the wash is to remove the receptors that have non-specifically bound to the incorrect ligands – such complexes would obviously not be present in the scenario proposed by Applicant . . . Further, the skilled artisan appreciates that the act of cell sorting with FACS constitutes an analysis of the receptor/ligand in real-time.

However, the Examiner has cited no prior art in support of the Examiner's assertion that the wash step in Dower is only inherent to the "particular application of the general method" of Dower. The only example of a flow cytometry process not requiring a wash step mentioned by the Examiner is Applicants' claimed method and Applicants' description of Applicants' invention may not be used as a reference. As held in *In Re Lee*, "It is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to '[use] that which the inventor taught against its teacher.'" (*See* 61 USPQ2d at 1434 (quoting *W.L. Gore v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983))). Therefore, the rejection of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 based on the combination of Baumbach and Dower is also improperly based on Applicants' description of Applicants' claimed invention, and the combination of Baumbach and Dower cannot teach or suggest the methods of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57.

Thus, as shown above, Baumbach and Dower, alone or in combination, fail to teach or suggest every feature of claim 1. Therefore, claim 1 is patentable over the combination of Baumbach and Dower.

Claims 6, 9-13, 15-17 and 54-57 depend directly or indirectly from claim 1, and, accordingly, include all of the patentable features of claim 1 as well as other patentable features. Therefore, claims 6, 9-13, 15-17 and 54-57 are patentable over the combination of Baumbach and Dower for at least the reasons discussed above with respect to claim 1.

Furthermore, with respect to claim 54, the Final Action cites no reference that teaches or suggests claim 54's feature of the step of incorporating an attachment tether to a receptor comprising incorporating at least one epitope tag. The Final Action merely states at page 4 that "claims 54-57 require that the tag be an epitope tag, e.g. either an N or C-terminal epitope. One of ordinary skill in the art appreciates that at col 20, first paragraph, U.S. Patent No. 5638603 [Dower] refers to such attachment means in the statement 'Solid phase assays can involved receptor attached to solid support either chemically or immunologically...'." However, the Final Action cites no prior art indicating that one of ordinary skill in the art would understand the cited paragraph to teaches or suggest claim 54's feature of the step of incorporating an attachment tether to a receptor comprising incorporating at least one epitope tag. Therefore, claim 54 is patentable over the combination of Baumbach and Dower for this additional reason.

Furthermore, with respect to claim 55, the Final Action cites no reference that teaches or suggests claim 55's feature of the step of incorporating an attachment tether

to a receptor comprising incorporating an N-terminal epitope tag. The Final Action merely states at page 4 that "claims 54-57 require that the tag be an epitope tag, e.g. either an N or C-terminal epitope. One of ordinary skill in the art appreciates that at col 20, first paragraph, U.S. Patent No. 5638603 [Dower] refers to such attachment means in the statement 'Solid phase assays can involved receptor attached to solid support either chemically or immunologically...'." However, the Final Action cites no prior art indicating that one of ordinary skill in the art would understand the cited paragraph to teaches or suggest claim 55's feature of the step of incorporating an attachment tether to a receptor comprising incorporating at least one epitope tag. Therefore, claim 55 is patentable over the combination of Baumbach and Dower for this additional reason.

Furthermore, with respect to claim 56, the Final Action cites no reference that teaches or suggests claim 56's feature of the step of incorporating an attachment tether to a receptor comprising incorporating a C-terminal epitope tag. The Final Action merely states at page 4 that "claims 54-57 require that the tag be an epitope tag, e.g. either an N or C-terminal epitope. One of ordinary skill in the art appreciates that at col 20, first paragraph, U.S. Patent No. 5638603 [Dower] refers to such attachment means in the statement 'Solid phase assays can involved receptor attached to solid support either chemically or immunologically...'." However, the Final Action cites no prior art indicating that one of ordinary skill in the art would understand the cited paragraph to teaches or suggest claim 56's feature of the step of incorporating an attachment tether to a receptor comprising incorporating at least one epitope tag. Therefore, claim 56 is patentable over the combination of Baumbach and Dower for this additional reason.

Furthermore, with respect to claim 57, the Final Action cites no reference that teaches or suggests claim 57's feature of the step of incorporating an attachment tether to a receptor comprising incorporating an internal epitope tag. The Final Action merely states at page 4 that "claims 54-57 require that the tag be an epitope tag, e.g. either an N or C-terminal epitope. One of ordinary skill in the art appreciates that at col 20, first paragraph, U.S. Patent No. 5638603 [Dower] refers to such attachment means in the statement "Solid phase assays can involved receptor attached to solid support either chemically or immunologically...'." However, the Final Action cites no prior art indicating that one of ordinary skill in the art would understand the cited paragraph to teaches or suggest claim 57's feature of the step of incorporating an attachment tether to a receptor comprising incorporating at least one epitope tag. Therefore, claim 55 is patentable over the combination of Baumbach and Dower for this additional reason.

With respect to claim 48, claim 48 claims a method for non-cellular display of 7-transmembrane receptors comprising: a) incorporating an attachment means to a receptor; b) solubilizing the receptor; c) presenting the receptor in conjunction with a support; d) presenting at least one ligand to bind to the receptor, wherein said ligand is known to bind to the receptor; e) combining the receptor and ligand to accomplish binding while the receptor is bound to the support; and f) sorting the bound receptor ligand pairs by fluorescence and using flow cytometry to analyze the fluorescence and binding interactions in real-time. However, at a minimum, the Baumbach and Dower fail to teach or suggest analyzing with a flow cytometer in real-time as recited in claim

48, and therefore; claim 48 is patentable over Baumbach and Dower, alone or in combination.

As admitted in the Office Action at page 4, Baumbach "appears to be silent with regard to flow cytometry." Thus, in an attempt to remedy the deficiencies of Baumbach, Dower is cited for teaching the general applicability of flow cytometry to the sorting of receptors and bound ligands. However, the general methodology and the flow cytometric analysis of Dower is very different from that recited in claim 48.

Dower provides for solubilization of a molecular or ligand library and display of the library on beads. The bead-bound library is then placed in contact with labeled receptors. A washing step is employed to remove unbound or non-specifically bound receptors. Then, a flow cytometer is used to identify and isolate individual beads showing high fluorescence. (*See* Dower, Col. 31, line 42+).

Claim 48 differs in several respects. Dower solubilizes and binds a ***ligand library*** to a bead. However, claim 48 recites the solubilization and subsequent attachment via a tether of a ***receptor*** to a bead. The solubilization and binding of the ***receptor*** allows the flow cytometric analysis to be carried out in real-time (*i.e.*, without the need for a washing step.) On the other hand, the binding of receptors in solution to an unknown ligand library discussed in Dower, requires a washing step to remove unbound or non-specifically bound receptors before analyzing with a flow cytometer. This extra step (or steps) adds time and the possibility for error in the analysis step. Through this process, Dower seeks to determine the identity of the bound ligand within the ligand library and thus seeks the areas of high fluorescence for isolation. However,

in claim 48, it is a known receptor that is bound to the bead and it is the interaction with the bound receptor that is analyzed.

Thus, as shown above, Baumbach and Dower, alone or in combination, fail to teach or suggest every feature of claim 48. Therefore, claim 48 is patentable over the combination of Baumbach and Dower. Thus, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 51 and 53 depend directly from claim 48, and, accordingly, include all of the patentable features of claim 48 as well as other patentable features. Therefore, claims 51 and 53 are patentable over Baumbach for at least the reasons discussed above with respect to claim 48.

(3) Whether the rejection under 35 U.S.C. § 103(a) of claims 2-5 and 8 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower), and further in view of Robeva should be withdrawn as improper and claims 2-5 and 8 allowed, because the combination of Robeva with Dower and Baumbach is improper.

As discussed above, with respect to the rejection under 35 U.S.C. § 103(a) of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower), the combination of Dower with Baumbach is improper. Therefore, because the combination of Dower with Baumbach is improper, the combination of Robeva with

the combination of Dower and Baumbach must also be improper. Therefore, the rejection under 35 U.S.C. § 103(a) of claims 2-5 and 8 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower), and further in view of Robeva should be withdrawn as improper and claims 2-5 and 8 allowed, because the combination of Robeva with Dower and Baumbach is improper.

(4) Whether the rejection under 35 U.S.C. § 103(a) of claims 2-5 and 8 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower), and further in view of Robeva should be withdrawn as improper and claims 2-5 and 8 allowed, because the combination of Robeva with Dower and Baumbach fails to teach or suggest the methods of claims 2-5 and 8.

Claims 2-5 and 8 depend directly or indirectly from claim 1, and, accordingly, include all of the patentable features of claim 1 as well as other patentable features. Therefore, claims 2-5 and 8 are patentable over the combination of Baumbach and Dower for at least the reasons discussed above with respect to claim 1. Robeva is only cited for teaching "that the step of incorporating an attachment scheme comprises incorporating the tag (coding sequence) into an oligonucleotide." (*See* Office Action, p. 7). Therefore, Robeva fails to remedy the deficiencies of the combination of Baumbach and Dower with respect to failing to teach or suggest the feature of carrying out a flow cytometric analysis in real-time as claimed by claims 2-5 and 8. Therefore, claims 2-5 and 8 are patentable over the combination of Robeva with

Baumbach and Dower.

(5) Claims 1-6, 8-13, 15-7, 48, 51, and 53-57 have been rejected upon facts within the personal knowledge of the Examiner, and Applicants hereby request under 37 C.F.R. § 1.104(d)(2) that the Examiner provide an affidavit supporting the Examiner's assertions used as a basis for the rejections of these claims

With respect to claims 1-6, 8-13, 15-7, 48, 51, and 53-57, these claims have also been rejected on the basis of facts within the personal knowledge of the Examiner. At pages 5-6 of the Office Action, the Examiner states:

> The wash step contemplated by Dower at line 60 col 31 is inherent to that particular application of the general method. If one were using the method of Dower to analyze the interaction between a receptor and it's known ligand, as Applicant points out, then a wash step would obviously not be required. The purpose of the wash is to remove the receptors that have non-specifically bound to the incorrect ligands – such complexes would obviously not be present in the scenario proposed by Applicant . . . Further, the skilled artisan appreciates that the act of cell sorting with FACS constitutes an analysis of the receptor/ligand in real-time.

However, the Examiner has cited no prior art in support of the Examiner's assertion that the wash step in Dower is only inherent to the "particular application of the general method" of Dower. The only example of a flow cytometry process not requiring a wash step mentioned by the Examiner is Applicants' claimed method and Applicants' description of Applicants' invention may not be used as a reference. As held in *In Re Lee*, "[i]t is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to '[use] that which the inventor

taught against its teacher.'" (*See* 61 USPQ2d at 1434 (quoting *W.L. Gore v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983))). Accordingly, under 37 C.F.R. § 1.104(d)(2) the Applicants hereby request that the Examiner provide an affidavit supporting the Examiner's assertion used as a basis for this rejection of claims 1-6, 8-13, 15-7, 48, 51, and 53-57 or withdraw the rejection. The above-cited grounds for rejecting claims 1-6, 8-13, 15-7, 48, 51, and 53-57 was set forth for the first time in the Final Action, so the Applicants have had no previous opportunity to request an affidavit under 37 C.F.R. § 1.104(d)(2) with respect to this grounds of rejection.

With respect to claims 54-57, these claims have been rejected on the basis of facts within the personal knowledge of the Examiner for an additional reason. At page 4 of the Office Action, the Examiner states that "claims 54-57 require that the tag be an epitope tag, e.g. either an N or C-terminal epitope. One of ordinary skill in the art appreciates that at col 20, first paragraph, U.S. Patent No. 5638603 [Dower] refers to such attachment means in the statement "Solid phase assays can involved receptor attached to solid support either chemically or immunologically...'." However, the Examiner has cited no prior art in support of the Examiner's claim that a person of ordinary skill in the art would so appreciate col. 20, first paragraph of Dower. Accordingly, under 37 C.F.R. § 1.104(d)(2) the Applicants hereby request that the Examiner provide an affidavit supporting the Examiner's assertion used as a basis for this rejection of claims 54-57 or withdraw the rejection. The rejection of claims 54-57 was made for the first time in the Final Action, so the Applicants have had no previous opportunity to request an affidavit under 37 C.F.R. § 1.104(d)(2) with

respect to the rejection of claims 54-57.

CONCLUSION

For the reasons discussed above, the rejection under 35 U.S.C. § 103(a) of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower) should be withdrawn as improper and claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57 allowed, because the combination of Dower with Baumbach is improper and because the combination of Dower with Baumbach fails to teach or suggest the methods of claims 1, 6, 9-13, 15-17, 48, 50, 51 and 53-57.

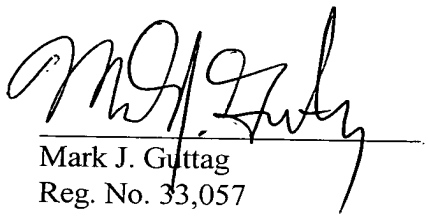
Also, for the reasons discussed above, the rejection under 35 U.S.C. § 103(a) of claims 2-5 and 8 as being unpatentable over U.S. Patent No. 5,583,010 (Baumbach) in view of U.S. Patent No. 5,639,603 (Dower), and further in view of Robeva should be withdrawn as improper and claims 2-5 and 8 allowed, because the combination of Robeva with Dower and Baumbach is improper and because the combination of Robeva with Dower and Baumbach fails to teach or suggest the methods of claims 2-5 and 8.

In addition, as requested above, the Examiner should provide an affidavit under 37 C.F.R. § 1.104(d)(2) supporting the Examiner's assertions based on his own personal knowledge used as a grounds for the rejection claims 1-6, 8-13, 15-17, 48, 50, 51 and 53-57 or withdraw the rejections of claims 1-6, 8-13, 15-17, 48, 50, 51 and 53-57.

Applicants' brief is submitted in triplicate, in accordance with 37 C.F.R. § 1.192(a). In addition, any references relied upon are attached to the present appeal brief in triplicate.

Please charge any additional fees due or credit any overage to Deposit Account 10-0233-UNME-0078-1.

Respectfully submitted,



Mark J. Guttag
Reg. No. 33,057

May 19, 2003

JAGTIANI + GUTTAG
10363-A Democracy Lane
Fairfax, VA 22030
(703) 591-2664

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:	)	
	)	
SKLAR *et al.*	)	**Examiner: Brannock, M.**
	)	
Serial Number: 09/370,358	)	**Art Unit: 1646**
	)	
Filed: August 9, 1999	)	
	)	
For: DISPLAY OF RECEPTORS AND ANALYSIS OF BINDING INTERACTIONS AND DRUG LIBRARIES	)	**Docket No.: UNME-0078-1**

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPENDIX A

Sir:

Claims 1-6, 8-13, 15-17, 48, 51 and 53-57 are currently pending in the present application. Claims 14 and 18-47 have been withdrawn from consideration. Please find below a clean copy of the claims that are presently pending in the current application:

1. A method for non-cellular analysis and display of 7-transmembrane receptors comprising the following steps:

a) incorporating an attachment tether to a receptor;

b) solubilizing the receptor; and

c) presenting the receptor in conjunction with a support, wherein said support comprises at least one substrate selected from the group consisting of silica bead substrates, latex bead substrates and other bead substrates appropriate for flow cytometry, and wherein the receptor in conjunction with a support is analyzed with a flow cytometer in real-time.

2. The method of claim 1 wherein the step of incorporating an attachment tether to a receptor comprises incorporating at least one of the following tags from the group consisting of C-Histidine, N-Histidine, biotin, and GST tags.

3. The method of claim 1 wherein the step of incorporating an attachment tether to a receptor comprises incorporating a tag into an oligonucleotide.

4. The method of claim 1 wherein the step of incorporating an attachment tether to a receptor comprises incorporating a tag into a GPCR construct prior to amplification.

5. The method of claim 1 wherein the step of solubilizing the receptor comprises solubilizing by lysing cell membranes containing the receptor.

6. The method of claim 1 wherein the step of presenting the receptor in conjunction with a support comprises presenting by affinity coupling the receptor to a particulate substrate.

8. The method of claim 1 wherein the step of presenting the receptors in conjunction with a support comprises presenting on a support comprising a Ni^{2+} silica bead.

9. The method of claim 1 wherein the step of presenting the receptors in conjunction with a support comprises presenting a fluorescently labeled receptor.

10. The method of claim 1 further comprising the step of (d) presenting at least one ligand to bind to the receptor, wherein said ligand is known to bind to the receptor.

11. The method of claim 10 wherein the step of presenting at least one ligand to bind to the receptor comprises presenting at least one fluorescently labeled ligand.

12. The method of claim 10 wherein the step of presenting at least one ligand to bind the receptor comprises presenting a library of ligands.

13. The method of claim 10 wherein the step of presenting at least one ligand to bind the receptor comprises presenting at least one ligand on a support.

15. The method of claim 10 further comprising the step of (e) combining the receptor and ligand to accomplish binding.

16. The method of claim 15 further comprising the step of (f) sorting the bound receptor ligand pairs by fluorescence.

17. The method of claim 16 wherein the step of sorting the bound receptor ligand pairs by fluorescence comprises sorting the bound receptor ligand pairs by flow cytometry.

48. A method for non-cellular display of 7-transmembrane receptors comprising the following steps:

a) incorporating an attachment means to a receptor;

b) solubilizing the receptor;

c) presenting the receptor in conjunction with a support;

d) presenting at least one ligand to bind to the receptor, wherein said ligand is known to bind to the receptor;

e) combining the receptor and ligand to accomplish binding while the receptor is bound to the support; and

f) sorting the bound receptor ligand pairs by fluorescence and using flow cytometry to analyze the fluorescence and binding interactions in real-time.

51. The method of claim 48, wherein said step of sorting the bound receptor pairs by fluorescence is carried out while the receptor is bound to the support.

53. The method of claim 48, wherein said support comprises at least one substrate selected from the group consisting of silica bead substrates, latex bead substrates and other bead substrates appropriate for flow cytometry.

54. The method of claim 1 wherein the step of incorporating an attachment tether to a receptor comprises incorporating at least one epitope tag.

55. The method of claim 54 wherein said at least one epitope tag is an N-terminal tag.

56. The method of claim 54 wherein said at least one epitope tag is a C-terminal tag.

57. The method of claim 54 wherein said at least one epitope tag is an internal tag.